

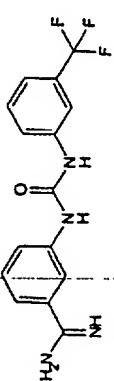
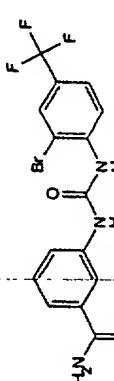
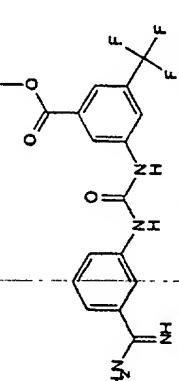
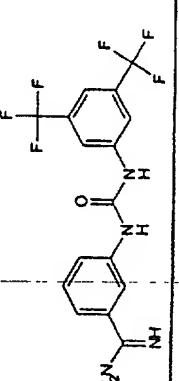
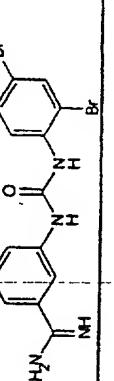
57

TABLE 1

N.	structure	synthesis method	MS	anti-plasmodial activity (Dd2)	anti-plasmodial activity (3D7)	human proteasome inhibition
1		2	316[M+H]	B		
2		2	323[M+H]	B		C (5 μM)
3		2	334[M+H]	B		
4		4	280[M+H]	B		

58

	4	300[M+H]	C	B				
5								
6		4 390[M+H]	C					
7		2 301[M+H]	B					
8		4 323[M+H]	B					
9		4 358[M+H]	A					

10		4	323[M+H]	B	B		
11		4	402[M+H]	B			
12		4	381[M+H]	B			
13		4	391[M+H]	B	B		
14		4	413[M+H]	B			

15		4	391[M+H] 389[M-H]	B	B		
16		4	381[M+H] 379[M-H]	B			
17		4	338[M+H]	C			
18		4	343[M+H]	A	A		
19		4	370[M+H]	B			

	3 450[M+H] B	3 390[M+H] B	9 447[M+H] B(5 μM)	3 468[M+H] C	3 500[M+H] A
20					
21					
22					
23					
24					

62

	4	334[M+H]	C	C	A(50 μ M)*
25					
26		4 378[M+H]	A	B	
27		3 410[M+H]	B		A(50 μ M)
28		3 546[M+H]	B		

64

34		2a	424[M+H] 422[M-H]	C	A	A(50 μ M) A(5 μ M)*		
35		9	424[M+H] 422[M-H]	A				
36		8	424[M+H] 422[M-H]	B				
37		8	424[M+H] 422[M-H]	A				
38		8	424[M+H]	A	B	A(50 μ M) A(5 μ M)*		

65

39	9 508[M+H] 506[M-H] [*]	A	B				
40	9 503[M+H] 501[M-H] [*]	A	A	A(50 μ M)*			
41	8 442[M+H] 440[M-H] [*]	A		A(50 μ M)*			
42	9 442[M+H] 440[M-H] [*]	A		A(50 μ M)			

67

		8 442[M+H] 440[M-H]	A A(50 μ M)*		
		478[M+H]	A(50 μ M)		
46					
47					
48		9 478[M+H]	B A(50 μ M)*		
49		9 460[M+H] 458[M-H]	A A(5 μ M)*		

68

	9 460[M+H] 458[M-H] 50	9 460[M+H] 458[M-H] 51	9 460[M+H] 458[M-H] 52	8 510[M+H] 50
	B	B	A	B
A(5 μ M)*				

69

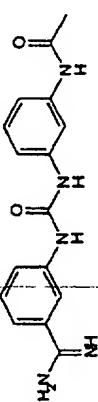
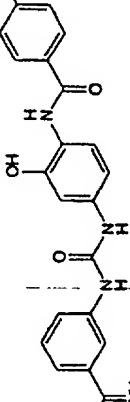
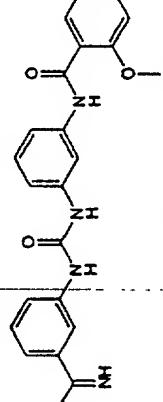
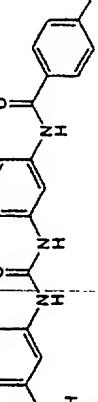
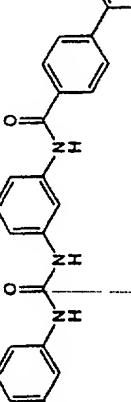
72

		9 460[M+H] 458[M-H]	A A(5 μM)*		
65					
66					
67					
68					
		9 460[M+H] 458[M-H]	A A(5 μM)*		
		9 478[M+H]	A A		
		8 442[M+H] 440[M-H]	B B(5 μM)		

		A(5 μ M)			
	8	503[M+H] 501[M-H]	B		
	9	469[M+H] 467[M-H]	A	A(5 μ M)*	
	3	529[M+H]	B		A(50 μ M)
69					
70					
71					

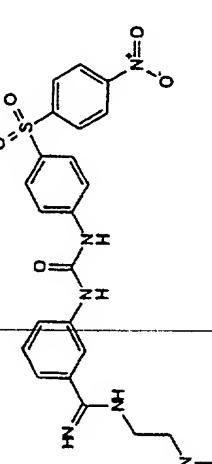
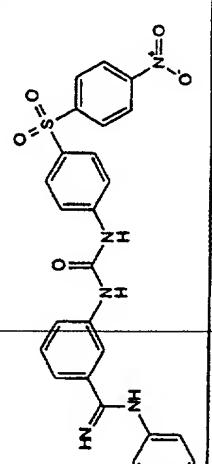
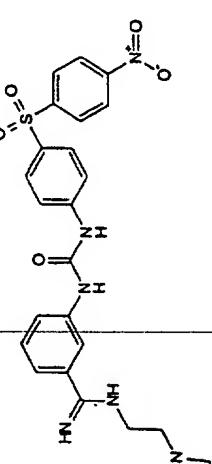
74

	4	395[M+H] B	B	
72				
73		4	395[M+H] B	B
74		8	440[M+H] A	B(5 μM)*
75		4	395[M+H] 393[M-H] A	B
76		4	454[M+H] B	

77	4 312[M+H] 	B			
78	4 404[M+H] 	B	B		
79	2 404[M+H] 	B			
80	2 404[M+H] 	A			
81	2a 450[M+H] 	B			

	4a	457[M-H] A			
86		4a 359[M+H] A			
87		4a 469[M-H] B			
88		4a 508[M+H] A			
89		4a 506[M-H] A			

	4a	440[M+H]	A(50 μ M)				
90				4a	494[M+H]*		
91				4a	397[M+H]	A	
92				4a	370[M+H]	A	A(50 μ M)
93							

	7 511[M+H] 509[M-H] B		
94		7 517[M+H] A	
95		7 537[M+H] 536[M-H] B	
96			

80

	7 478[M+H] B						
101							
102		8 580[M+H] 578[M-H] B					
103			8 616[M+H] 614[M-H] A C				
104				7 349[M+H] 347[M-H] A		B (5 μM)	

	7 339[M+H] 337[M-H]			
105		7 436[M+H] 434[M-H]	8	
106			8 508[M+H] 506[M-H]	
107				8 440[M+H]
108				

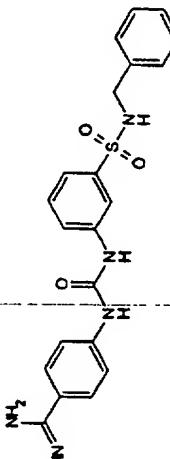
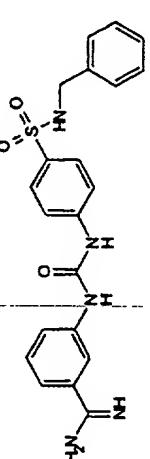
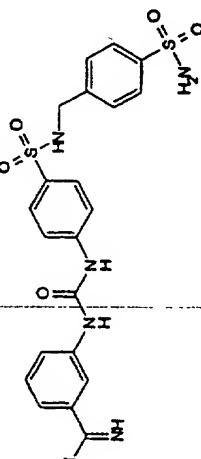
	B 519[M+H] 517[M-H]	C 607[M+H] 605[M-H]	
8			
109		110	111

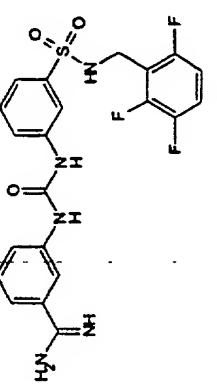
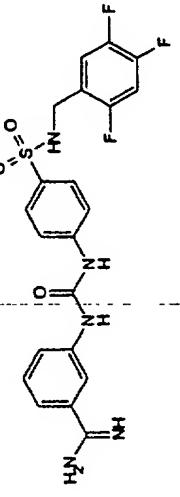
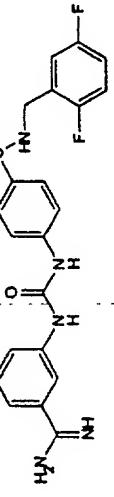
				A(50 μ M)
8	529[M+H] 527[M-H]	A	B	
7	473[M-H] 475[M+H]	B		
112				
113				
114				

85

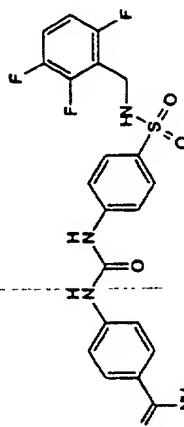
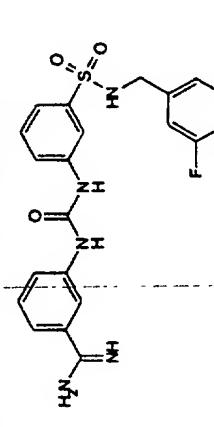
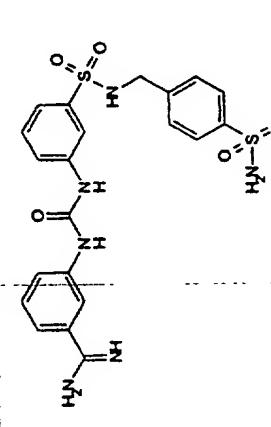
TABLE 2

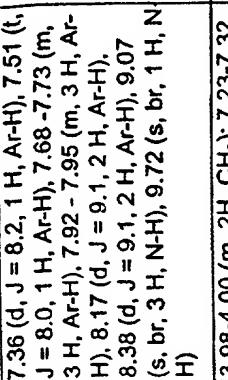
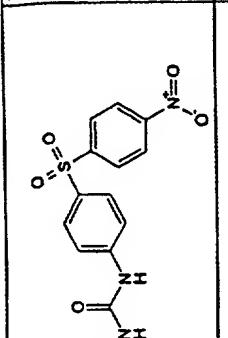
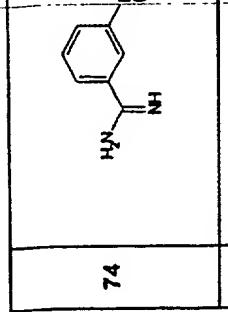
N	Structure	1H-NMR (D ₆ -DMSO)		13C-NMR
		Chemical Shift (ppm)	Integration	
24		5.54 (s, 1 H, Ph ₂ CH), 7.11-7.21 (m, 10 H, Ar-H), 7.42 (ddd, J = 7.8, 1.8 and 1.1 Hz, 1 H, 4-H) 7.45-7.58 (m, 5 H, Ar-H), 7.69-7.78 (ddd, J = 8.1, 1.8 and 1.1 Hz, 1 H, 6-H), 8.02 (t, J = 1.8 Hz, 1 H, 2-H)		
35		3.96 (d, J = 6.3, 2 H, CH ₂), 7.22-7.29 (m, 5 H, Ar-H), 7.64 (d, J = 8.9, 2 H, Ar-H), 7.69 (d, J = 9.0, 2 H, Ar-H), 7.74 (d, J = 9.0, 2 H, Ar-H), 7.81 (d, J = 8.9, 2 H, Ar-H), 8.0 (t, J = 6.3, 1 H, N-H), 8.82 (s, 2 H, N-H), 9.18 (s, 2 H, N-H), 9.92 (s, 1 H, N-H), 10.00 (s, 1 H, N-H)		
36		3.99 (d, J = 6.3, 2 H, CH ₂), 7.23-7.30 (m, 5 H, Ar-H), 7.36 (d, J = 8.3, 1 H, Ar-H), 7.40-7.43 (m, 1 H, Ar-H), 7.47-7.56 (m, 2 H, Ar-H), 7.58-7.61 (m, 1 H, Ar-H), 7.72-7.75 (m, 1 H, Ar-H), 7.98 (t, J = 1.8, 1 H, Ar-H), 8.12 (t, J = 1.8, 1 H, Ar-H), 8.19 (t, J = 6.3, 1 H, N-H), 9.00 (s, 2 H, N-H), 9.35 (s, 2 H, N-H), 9.77 (s, 1 H, N-H), 9.82 (s, 1 H, N-H)		

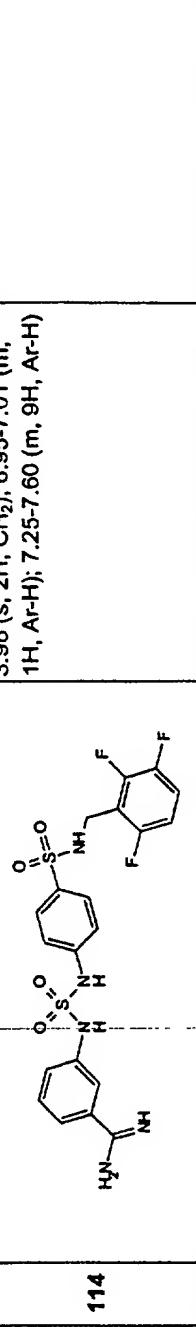
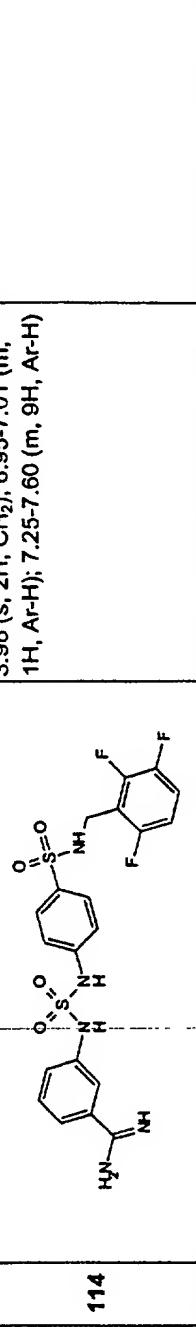
<p>3.99 (d, J = 6.3, 2 H, CH_2), 7.24-7.39 (m, 5 H, Ar-H), 7.42 (d, J = 7.9, 1 H, Ar-H), 7.50 (t, J = 7.9, 1 H, Ar-H), 7.59 (d, J = 7.9, 1 H, Ar-H), 7.70 (d, J = 8.9, 2 H, Ar-H), 7.81 (d, J = 8.9, 2 H, Ar-H), 8.09 (t, J = 1.8, 1 H, Ar-H), 8.12 (t, J = 1.8, 1 H, Ar-H), 8.19 (t, J = 6.3, 1 H, N-H), 8.83 (s, 2 H, N-H), 9.18 (s, 2 H, N-H), 9.85 (s, 1 H, N-H), 10.02 (s, 1 H, N-H)</p> <p>37</p> 	<p>3.95 (d, J = 6.3, 2 H, CH_2), 7.21-7.30 (m, 5 H, Ar-H), 7.37 (d, J = 8.1, 1 H, Ar-H), 7.52 (t, J = 7.8, 1 H, Ar-H), 7.64 (d, J = 9.0, 2 H, Ar-H), 7.71 - 7.75 (m, 3 H, Ar-H), 7.95 (t, J = 2.1, 1 H, Ar-H), 7.99 (t, J = 6.3, 1 H, N-H), 9.13, (s, 2 H, N-H), 9.38 (s, 2 H, N-H), 10.08 (s, 1 H, N-H), 10.23 (s, 1 H, N-H)</p> <p>38</p> 	<p>3.96 (s, 2 H, CH_2), 7.29 - 7.39 (m, 3 H, Ar-H), 7.45 - 7.50 (m, 1 H, Ar-H), 7.59 - 7.69 (m, 7 H, Ar-H), 7.89 (s, 1 H, Ar-H), 9.73 (s, 1 H, N-H), 9.88 (s, 1 H, N-H)</p> <p>40</p> 
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<p>47</p>  <p>4.05-4.06 (d, 2H, CH_2); 6.99-7.07 (m, 1H, FAr); 7.33-7.74 (m, 7H, Ar); 7.96 (s, 1H, o-Ar); 8.05 (s, 1H, o-Ar); 8.28 (t, 1H, NH); 9.04 (s, 2H, NH); 9.35 (s, 2H, NH); 9.86 (s, 1H, NH); 9.89 (s, 1H, NH)</p>	<p>3.99 (s, 2H, CH_2); 7.29-7.73 (m, 10H, Ar); 7.95 (s, 1H, Ar); 9.18 (m br, 3H, C(NH)NH2); 9.69 (s, 1H, NH); 9.82 (s, 1H, NH)</p>	<p>4.02 (s, 2H, CH_2); 7.11 - 7.18 (m, 3H, Ar-H); 7.37 (d, J = 8.3, 1H, Ar-H); 7.54 (t, J = 8.0, 1H, Ar-H); 7.63 (d, J = 9.1, 2H, Ar-H); 7.69 - 7.75 (m, 3H, Ar-H); 7.96 (s, 1H, Ar-H); 9.05 (s, br, 3H, N-H); 9.83 (s, 1H, N-H); 9.97 (s, 1H, N-H)</p>
<p>48</p>  <p>3.99 (s, 2H, CH_2); 7.29-7.73 (m, 10H, Ar); 7.95 (s, 1H, Ar); 9.18 (m br, 3H, C(NH)NH2); 9.69 (s, 1H, NH); 9.82 (s, 1H, NH)</p>	<p>4.02 (s, 2H, CH_2); 7.11 - 7.18 (m, 3H, Ar-H); 7.37 (d, J = 8.3, 1H, Ar-H); 7.54 (t, J = 8.0, 1H, Ar-H); 7.63 (d, J = 9.1, 2H, Ar-H); 7.69 - 7.75 (m, 3H, Ar-H); 7.96 (s, 1H, Ar-H); 9.05 (s, br, 3H, N-H); 9.83 (s, 1H, N-H); 9.97 (s, 1H, N-H)</p>	<p>4.02 (s, 2H, CH_2); 7.11 - 7.18 (m, 3H, Ar-H); 7.37 (d, J = 8.3, 1H, Ar-H); 7.54 (t, J = 8.0, 1H, Ar-H); 7.63 (d, J = 9.1, 2H, Ar-H); 7.69 - 7.75 (m, 3H, Ar-H); 7.96 (s, 1H, Ar-H); 9.05 (s, br, 3H, N-H); 9.83 (s, 1H, N-H); 9.97 (s, 1H, N-H)</p>
<p>49</p>  <p>3.99 (s, 2H, CH_2); 7.29-7.73 (m, 10H, Ar); 7.95 (s, 1H, Ar); 9.18 (m br, 3H, C(NH)NH2); 9.69 (s, 1H, NH); 9.82 (s, 1H, NH)</p>	<p>4.02 (s, 2H, CH_2); 7.11 - 7.18 (m, 3H, Ar-H); 7.37 (d, J = 8.3, 1H, Ar-H); 7.54 (t, J = 8.0, 1H, Ar-H); 7.63 (d, J = 9.1, 2H, Ar-H); 7.69 - 7.75 (m, 3H, Ar-H); 7.96 (s, 1H, Ar-H); 9.05 (s, br, 3H, N-H); 9.83 (s, 1H, N-H); 9.97 (s, 1H, N-H)</p>	<p>4.02 (s, 2H, CH_2); 7.11 - 7.18 (m, 3H, Ar-H); 7.37 (d, J = 8.3, 1H, Ar-H); 7.54 (t, J = 8.0, 1H, Ar-H); 7.63 (d, J = 9.1, 2H, Ar-H); 7.69 - 7.75 (m, 3H, Ar-H); 7.96 (s, 1H, Ar-H); 9.05 (s, br, 3H, N-H); 9.83 (s, 1H, N-H); 9.97 (s, 1H, N-H)</p>

<p>3.96 (d, J = 6.3, 2 H, CH₂), 7.98 - 7.05 (ddd, J = 8.5, J = 8.5, J = 2.5, J = 1.0, 1 H, Ar-H), 7.10 - 7.17 (ddd, J = 10.4, J = 9.5, J = 2.6, 1 H, Ar-H), 7.33 - 7.41 (m, 2 H, Ar-H), 7.53 (t, J = 8.0, 1 H, Ar-H), 7.63 (d, J = 9.1, 2 H, Ar-H), 7.68 - 7.74 (m, 3 H, Ar-H), 7.95 (t, J = 1.8, 1 H, Ar-H), 9.05 (t, J = 6.2, 1 H, N-H), 8.98 (s, 2 H, N-H), 9.34 (s, 2 H, N-H), 9.77 (s, 1 H, N-H), 9.90 (s, 1 H, N-H)</p>	<p>3.98 (s, 2 H, CH₂), 7.09 - 7.12 (m, 1 H, Ar-H), 7.22 - 7.38 (m, 3 H, Ar-H), 7.54 (t, J = 8.0, 1 H, Ar-H), 7.63 (d, J = 9.1, 2 H, Ar-H), 7.69 - 7.75 (m, 3 H, Ar-H), 7.96 (s, 1 H, Ar-H), 9.10 (s, br, 3 H, N-H), 9.81 (s, 1 H, N-H), 9.95 (s, 1 H, N-H)</p>	<p>3.94 (d, J = 5.7, 2 H, CH₂), 6.97 (t, J = 8.0, 2 H, Ar-H), 7.26 - 7.36 (m, 2 H, Ar-H), 7.49 (t, J = 8.0, 1 H, Ar-H), 7.58 (d, J = 9.0, 2 H, Ar-H), 7.68 - 65 (d, J = 9.0, 2 H, Ar-H) 7.68 - 7.71 (m, 1 H, Ar-H), 7.91 - 7.94 (m, 2 H, Ar-H, N-H), 9.02 (s, 2 H, N-H), 9.32 (s, 2 H, N-H), 9.91 (s, 1 H, N-H), 10.05 (s, 1 H, N-H)</p>
<p>50</p>	<p>51</p>	<p>52</p>

<p>4.01 (d, J = 5.3, 2 H, CH₂), 7.01 - 7.07 (m, 1 H, Ar-H), 7.34 - 7.45 (m, 1 H, Ar-H), 7.61 (d, J = 8.9, 2 H, Ar-H), 7.68 (d, J = 7.5, 4 H, Ar-H), 7.81 (d, J = 8.9, 2 H, Ar-H), 8.10 (t, J = 5.5, 1 H, N-H), 8.92 (s, 2 H, N-H), 9.20 (s, 2 H, N-H), 10.13 (s, 1 H, N-H), 10.23 (s, 1 H, N-H)</p> <p>67</p> 	<p>4.03 (d, J = 5.2, 2 H, CH₂), 7.02 - 7.12 (m, 3 H, Ar-H), 7.29 - 7.41 (m, 3 H, Ar-H), 7.46 - 7.59 (m, 3 H, Ar-H), 7.73 (d, J = 8.3, 1 H, Ar-H), 7.98 (s, 1 H, Ar-H), 8.12 (t, J = 1.9, 1 H, Ar-H), 8.27 (m, br, 1 H, N-H) 9.00 (s, br, 2 H, N-H), 9.35 (s, br, 2 H, N-H), 9.78 (s, br, 2 H, N-H)</p> <p>68</p> 	<p>4.05 (d, J = 6.1, 2 H, CH₂), 7.33 - 7.51 (m, 6 H, Ar-H), 7.62 (d, J = 8.9, 1 H, Ar-H), 7.73 - 7.76 (m, 3 H, Ar-H), 7.99 (t, J = 1.7, 1 H, Ar-H), 8.17 (t, J = 1.9, 1 H, Ar-H), 8.65 (s, br, 4 H, N-H), 10.4 (s, br, 2 H, N-H)</p> <p>69</p> 
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 <p>74</p>	<p>7.36 (d, J = 8.2, 1 H, Ar-H), 7.51 (t, J = 8.0, 1 H, Ar-H), 7.68 - 7.73 (m, 3 H, Ar-H), 7.92 - 7.95 (m, 3 H, Ar-H), 8.17 (d, J = 9.1, 2 H, Ar-H), 8.38 (d, J = 9.1, 2 H, Ar-H), 9.07 (s, br, 3 H, N-H), 9.72 (s, br, 1 H, N-H)</p>	<p>3.98-4.00 (m, 2H, CH₂); 7.23-7.32 (m, 5H, Ar); 7.58-7.63 (m, 2H, Ar); 7.76-7.89 (m, 2H, Ar); 7.92-7.94 (m, 3H, Ar); 8.06 (s, 1 H, Ar), 8.08-8.13 (t, 1H, NH); 9.14-9.41 (2 s, br, 3 H, C(NH)NH₂); 11.03-11.18 (2 s, 2 H, NH)</p>	<p>46.03 (Bz CH₂); 121.99-142.95 (C Ary); 165.58 (C(NH)NH₂); 179.44 (C=S)</p>
 <p>90</p>			
 <p>103</p>			
 <p>104</p>			

114	 <p>3.96 (s, 2H, CH_2); 6.95-7.01 (m, 1H, Ar-H); 7.25-7.60 (m, 9H, Ar-H)</p>	<p>4.07 (s, 2H, BnCH_2), 7.18-7.25 (m, 5H, Ph), 7.59 (dt, J = 7.8 and 1.7 Hz, 1H, 4-H), 7.64 (t, J = 7.8 Hz, 1H, 5-H), 7.83 (dt, J = 9.0 and 2.1 Hz, 2H, 3',5'-H), 7.96 (dt, J = 9.0 and 2.1 Hz, 2H, 2',6'-H), 7.69 (dt, J = 7.6 and 1.7 Hz, 1H, 6-H), 8.13 (t, J = 1.7 Hz, 1H, 2-H)</p>	<p>47.9 ($\text{CH}_2\text{-Bn}$), 120.7 (C-2), 121.5 (C-2',6'), 125.3 (C-4), 126.9 (C-6), 128.5 (C-4''), 128.9, 129.1 and 129.4 (C-3',5',2'',3''), 131.2 (C-5), 130.6, 138.2, 138.6, 139.7 and 142.3 (C-1,3,1',3',1''), 159.7 and 159.9 (C=O), 168.6 (C=NH)</p>
115		<p>4.02 (s, 2H, PhCH_2), 7.18-7.30 (m, 5H), 7.54-7.66 (m, 4H), 8.07-8.05 (m, 1H), 8.17 (dt, J = 7.1 and 2.0 Hz, 1H, (Ar-H), 8.29-8.31 (m, 1H) and 8.44-8.46 (m, 1H) (H-1 and H-1')</p>	<p>46.1 ($\text{CH}_2\text{-Ph}$), 118.5 and 119.9 (C-1 and C-1'), 122.4, 124.0, 124.2, 125.2, 127.0, 127.5, 128.1, 129.0, 129.5, 129.6, 137.6, 138.0, 138.0 (C-aromatic), 158.6 and 158.6 (O=C-N), 166.1 (N=C-N)</p>
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